DOCUMENT RESUME

ED 094 545 EC 062 714

TITLE	Antenatal Diagnosis and Down's Syndrome.
INSTITUTION	National Inst. of Child Health and Human Development (NIH), Bethesda, Md.
REPORT NO	DHEW-NIH-74-538
PUB DATE	73
NOTE	16p.; For related document addressed to women over 35 years old, see EC 062 715
AVAILABLE FROM	National Institute of Child Health and Human Development, Landow Building Room C-708, 7910 Woodmont Avenue, Bethesda, Maryland 20014 (Single copies)
EDRS PRICE	MF-$0.75 HC-$1.50 PLUS POSTAGE
DESCRIPTORS	*Diagnostic Tests; Etiology; *Exceptional Child Education; *Genetics; Mentally Handicapped; *Mongolism; *Parent Counseling

ABSTRACT

The pamphlet, written for physicians and other health professionals who counsel parents, explain five factors which put women at high risk of giving birth to a child with Down's Syndrome and three antenatal diagnostic techniques. Five factors identified as indicating high risk are advanced maternal age (over 40 years old), a previous child with Down's Syndrome, chromosomal translocation in mother or father, parental mosaicism, and Down's Syndrome in the mother. Briefly examined are the uses of amniocentesis, amniography, and ultrasonography as antenatal diagnostic techniques, the risks of amniocentesis, the benefits of proper diagnosis, and what parents can expect if they have a child with Down's Syndrome. (GW)

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antenatal diagnosis and down's syndrome

EC062714

The National Institute of
Child Health and Human Development (NICHD)
DHEW Publication No. (NIH) 74-538

It is a fact that maternal age is correlated with genetic defects in children. The chances of giving birth to a child with Down's syndrome,* for example, are five to ten times higher for women over 35.

Many physicians advise their patients to practice family planning in order to maximize the chances of having a healthy baby. Still, there are a significant number of women who bear children after the age of 35.

The NICHD has begun a campaign to inform women about the relationship of maternal age to genetic defects; and a simple, question and answer booklet is available to the public.** "Antenatal Diagnosis and Down's Syndrome," however, is designed primarily for the physician or other health professional, who must advise patients on a day-to-day basis.

The information in this pamphlet will be helpful in answering some of the additional questions which patients may ask about:

- "high-risk" mothers
- antenatal diagnostic procedures
- the risks of amniocentesis
- the benefits of proper diagnosis
- the child with Down's syndrome

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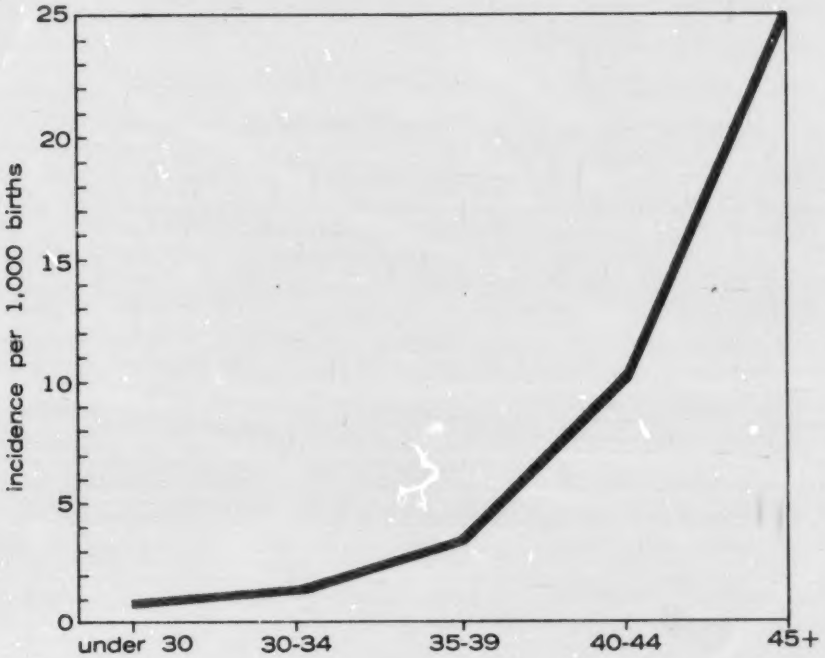
* Down's syndrome, also known as mongolism, is a genetic disease characterized by physical defects and mental deficiency, and is one of the most common causes of mental retardation. Down's syndrome (Trisomy 21) is evidenced by extra chromosomal material in pair 21 and is most often caused by nondisjunction in the male or female gamete during meiosis.

** "Facts About Mongolism For Women Over 35," Government Printing Office, Washington, D.C. 20402.

Relationship of Down's Syndrome to Maternal Age



The risk of having a child with Down's Syndrome increases with maternal age.

WHO IS "AT RISK" FOR PRODUCING A CHILD WITH DOWN'S SYNDROME?

Five factors put women at high risk of giving birth to a child with Down's syndrome. Women under your care, who fall into any of the following categories, should be considered for prenatal diagnosis of Down's syndrome.

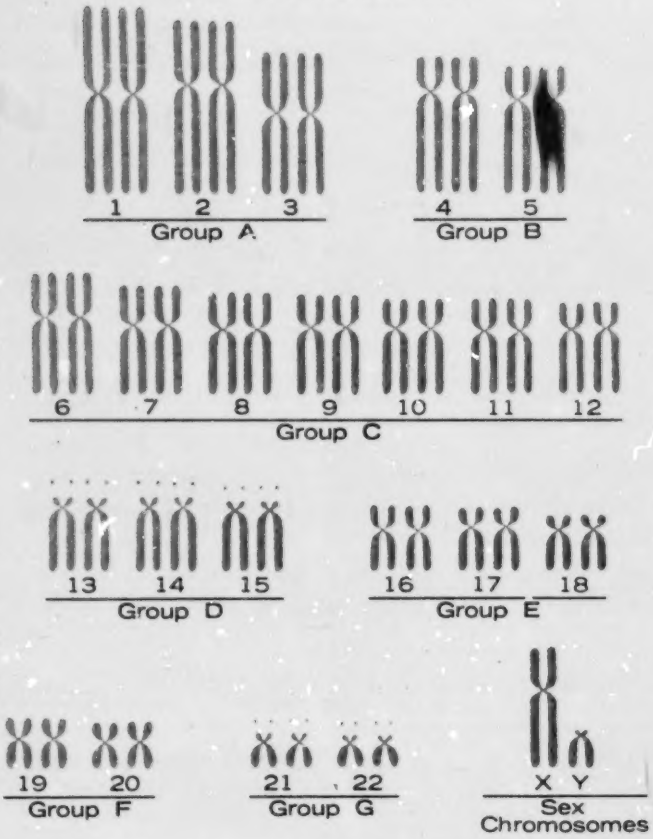
1. **Advanced maternal age (over 40):** The risk of giving birth to a child with Down's syndrome (Trisomy 21) for a woman between the ages of 40 and 45, is about 1:100; and 1:40 in the age group of 45 and over. By contrast, women under 30 years old have only a 1:1500 risk of having a child with mongolism. Women of advanced maternal age comprise the largest "high-risk" group.

2. **A previous child with Down's syndrome:** The recurrence risk for Down's syndrome (Trisomy 21) is about one percent, up to age 35.

3. **Familial translocation:**
   If the mother carries a translocation which involves the D/21 chromosomes,* the risk of producing a child with Down's syndrome is about 20 percent. If the father carries a similar translocation, the risk, for an unknown reason, is only around two percent. If, as in rare cases, either parent

* The D chromosomes include #13,14,15.

Normal Karyotype



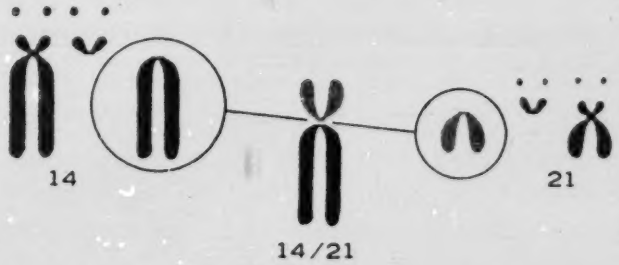
The autosomes are arranged in pairs according to the Denver system. Nos. 1, 2 and 3 are sometimes classified as Group A, 4 and 5 as Group B, 6 to 12 as Group C, 13 to 15 as Group D, 16 to 18 as Group E, 19 and 20 as Group F and 21 and 22 as Group G. The sex chromosomes are X and Y. Pairs 13, 14, 15, 21 and 22 carry small bodies, known as satellites, attached to the short arms.

carries a balanced 21/21 translocation, the risk increases to 100 percent.

4. **Parental mosaicism** with a 21 trisomic cell population: Fathers as well as mothers who possess chromosomal mosaicism with a 21 trisomic cell population have a high, although not precisely predictable risk of having more than one child with mongolism. However, the number of pregnancies in this group is also small.

5. **Down's syndrome:** For pregnant women affected with mongolism, the risk is 50 percent. However, pregnancies among women with mongolism are extremely rare.

Formation Of A Translocation Chromosome



A translocation occurs when a piece of one chromosome breaks off and attaches to a different chromosome. This "translocation chromosome" has been formed by the breaking and rejoining of chromosomes 14 and 21 (with loss of the little pieces).

WHAT ARE THE CURRENT ANTENATAL DIAGNOSTIC TECHNIQUES?

1. Amniocentesis:[1]

Amniocentesis was first developed in the latter part of the last century and consists of obtaining amniotic fluid through the insertion of a needle into the amniotic cavity. The cells in this fluid are fetal in origin and, therefore, represent the fetal chromosome and genetic complement. In the past, this technique has been used for studies of the biochemistry of the amniotic fluid and for the antenatal diagnosis of sex. In the middle 1960's, an increasing interest in fetology, a greater awareness of the possibilities of genetic diagnosis, and a change in attitudes toward therapeutic abortion led to a renewed surge of interest in amniocentesis.

Description: The transabdominal procedure (as opposed to the ... transcervical amniocentesis), is a relatively simple one. It is desirable to locate the placenta to avoid puncturing it with the needle. The bladder must be emptied, then the uterus is flexed anteriorly with one hand (two operators are sometimes required if the pregnancy is not sufficiently advanced or if the patient is obese), and a 20-23 gauge spinal needle and a syringe are used. In general local anesthesia is not required at the site of puncture if insertion is in the midline. If it is outside the midline, the skin is infiltrated with procaine hydrochloride. One can feel a slight resistance as the skin is punctured, then little resistance until the myometrium is reached. The patient's pain is minimal, but there is some discomfort as the needle

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[1] Information for these sections was drawn from **Antenatal Diagnosis**, Albert Dorfman, ed. © 1972 by The University of Chicago Press.

goes through the peritoneum. Beyond that point the procedure causes little pain except pressure and a deep hollow feeling which some patients experience if a significant quantity of amniotic fluid is withdrawn. When the needle is in the amniotic cavity, there is some positive pressure, and the fluid comes freely into the syringe. For the prenatal diagnosis of Down's syndrome, usually 10 to 20 cc. will be sufficient. However, the physician should first contact his laboratory to determine the amount of fluid required and mailing procedures. Many clinics prefer to have the amniocentesis performed nearby. Analysis of the amniotic fluid usually takes two or three weeks.

Further information about formal training programs in amniocentesis can be obtained through your local medical society or medical school.

2. Other antenatal diagnostic techniques:

Other antenatal diagnostic techniques are being developed and perfected. The following three procedures are still in the **experimental** stage, but they may become extremely useful in the diagnosis of anencephaly and other congenital abnormalities that cannot be detected through amniocentesis.

a. **Amniography*:** A contrast material, preferably water soluble, is injected into the amniotic fluid. The dye mixes with the amniotic fluid and thus provides a contrast to the fetus; an X-ray picture will show the outline of the fetus.

b. **Ultrasonography*:** This procedure employs the techniques of ultrasound and

* For further information on these research techniques, refer to the bibliography on page 15.

the application of the Doppler principle to study the fetus; it is often utilized to determine the location of the placenta prior to amniocentesis.

c. **Fetoscopy*:** This procedure involves the direct visualization of the fetus utilizing a fiberoptic endoscope. The current endoscope under development is flexible and only 2 mm. in diameter.

WHAT ARE THE RISKS OF AMNIOCENTESIS?[1]

The risks of amniocentesis for the mother are the classic triad of medicine: trauma, hemorrhage, and infection. Superficial skin hemorrhage or peritoneal hemorrhage is not normally associated with the procedure, and generally one cannot subsequently tell where the needle was inserted. Bleeding from the uterine wall seems to occur only where there are uterine varicosities, usually in the myometrium or at the external surface. Other bleeding can occur in the bladder or gut or abdominal wall when varicosities are present. However, adequate previous gynecological examination should obviate these risks. Difficulty is encountered only when there has been extensive pelvic surgery or previous extensive pelvic infection or abdominal surgery.

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(1) Information for these sections was drawn from **Antenatal Diagnosis,** Albert Dorfman, ed. © 1972 by The University of Chicago Press.

The risks to the fetus are also the triad of trauma, infection, and hemorrhage. Eight weeks after the first day of the last menstrual period (six weeks conceptual age), the amniotic cavity is less than ¾ inch in diameter. The volume of this cavity is less than 2.5 ml. At a menstrual age of 16 weeks (gestational age—14 weeks), the placenta still occupies about 50 percent of the surface area, but the amniotic cavity is much larger and the cellular content of the amniotic fluid is increased. This is the first stage at which amniocentesis may be performed with minimal fetal risk. At this time, the chances of penetrating the fetus and of pro-

Amniocentesis at 16-17 weeks.

ducing hemorrhage are decreased. In patients observed by various investigators, bloody taps were obtained at a frequency approaching eight percent, but no evidence has been presented of blood loss or hemorrhagic areas in the placenta. In no case was fetal blood detectable in the amniotic fluid on the basis of the presence of fetal hemoglobin.

The National Institute of Child Health and Human Development is currently supporting a three-year project designed to gather data on pregnancy and birth experience following amniocentesis. Approximately 1,000 women are being carefully followed through their pregnancies and deliveries; and physical examinations are administered to babies soon after birth and after one year. Final reports on this project should be completed about June 1975. Although the actual risks, both to the mother and the fetus, have yet to be documented for a large American population, amniocentesis appears to be a relatively safe procedure.

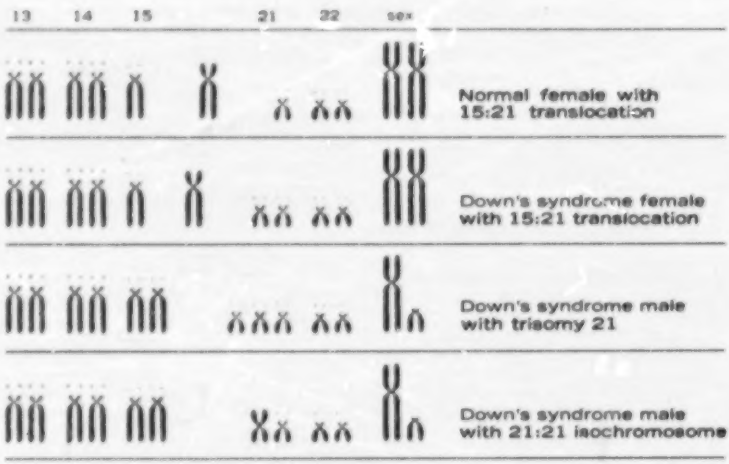
WHAT ARE THE BENEFITS OF PROPER DIAGNOSIS?

The benefits of antenatal diagnosis can be examined from many points of view—medical, ethical, economic, and so on. The most significant benefits are those perceived by couples facing a "high-risk" situation who, without the availability of amniocentesis, might needlessly choose to interrupt pregnancy. One case concerned a 31-year-old mother of a two-year-old child with Down's syndrome (Trisomy 21), who discovered that she had become pregnant again. After she learned that she had approximately a one percent chance of pro-

ducing another child with mongolism, she demanded an abortion. Her physician suggested that she undergo amniocentesis and prenatal chromosome analysis first, to determine whether or not the child would be affected. She agreed, and much to her relief, discovered that the fetus had a normal karyotype. The mother decided to complete the pregnancy and eventually delivered a normal baby.

WHAT CAN PARENTS EXPECT IF THEY HAVE A CHILD WITH DOWN'S SYNDROME?

The use of antibiotics and the development of modern heart surgery have increased the life expectancy of a child with Down's syndrome. The actual burden of the condition upon the family is difficult to assess, since it is so dependent upon



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Single copies are available from
National Institute of Child Health and Human Development
Landow Building Room C-708
7910 Woodmont Avenue
Bethesda, Maryland 20014

U. S. GOVERNMENT PRINTING OFFICE : 1973 O - 526-115

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
Public Health Service
National Institutes of Health
DHEW Publication No. (NIH) 74-538

the family's general outlook on life, the stability of a couple's marriage, and their expectations for their children. Society is becoming more understanding of mental retardation, and more sophisticated special education and vocational education programs are available. Generally speaking, children with mongolism will be severely to moderately retarded, with IQs in the 30s and 40s, but occasionally, in the 60s and 70s. As adults, they can carry out many tasks, either while living at home or in a supervised, non-institutional setting. There is no **cure** for Down's syndrome at this time, but if parents can accept the initial setback of learning that their child will not be "normal," it is possible for them to derive a great deal of happiness and enjoyment from their child.

FURTHER INFORMATION

As a physician, you may wish to examine, in greater depth, some aspects of antenatal diagnosis or Down's syndrome. The following bibliography has been compiled for this purpose.